Brief Summary of the Circulatory System Devices Panel Meeting – March 20, 2013

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on March 20, 2013 to make recommendations and vote on information related to the premarket approval application (100009) for the MitraClip Clip Delivery System sponsored by Abbott Vascular. The system consists of three major components: the Delivery Catheter, the Steerable Sleeve and the MitraClip device. The MitraClip device is a single sized, percutaneously implanted mechanical clip intended for the reduction of mitral regurgitation. The MitraClip device grasps and coapts the mitral valve leaflets resulting in fixed central tissue approximation of the mitral leaflets throughout the cardiac cycle. The implantable MitraClip device is fabricated with metal alloys and polyester fabric (clip cover) that are commonly used in cardiovascular implants.

The proposed indication for use for this PMA is: *The MitraClip Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR≥3+) in patients who have been determined by a cardiac surgeon to be too high risk for open mitral valve surgery and in whom existing co-morbidities would not preclude the expected benefit from correction of the mitral regurgitation.*

Panel Deliberations/FDA Questions:

Regarding the appropriateness of pooling the EVEREST II HRR and REALISM HR, the panel generally believed that the data were not poolable.

The panel agreed that using the STS score for mitral valve replacement is not a good comparator. However, if it were to be used, it is not clear why the STS score for mitral valve replacement rather than mitral valve repair would be better as the comparator.

The panel had a mixed response regarding using the STS score for mitral valve repair for selection of high surgical risk and inoperable patients. They leaned more in favor of using repair as selection criteria that should be supplemented by additional criteria not represented in STS score.

The panel believed that using the Duke database was somewhat reasonable to use as a comparator for mortality however, there are other large scale centers where the same hypothesis could be tested and a randomized trial would provide more robust data.

The panel was generally not opposed to using retrospective subset analysis for first-of-a kind devices for safety and effectiveness, however there was concern about the strength of evidence from these various sets of data in this specific situation because of a lack of a good control group.

The panel members generally agree with the FDA's following list, however there is a very small group of patients where this device could be beneficial, but with the current definition of the patients studied and use of these datasets, it's hard to distinguish who would benefit from the device.

1. The EVEREST II RCT did not demonstrate an appropriate benefit-risk profile when compared to standard mitral valve surgery in a selected mitral valve patient population.
2. The EVEREST II High Risk Registry was designed as an adjunctive single arm registry that was not intended to be used as a pivotal data set and is difficult to interpret.
3. REALISM High Risk Registry is a continued access protocol cohort that was designed as an adjunctive single arm registry that was not intended to be used as a pivotal data set and is difficult to interpret.
4. The Integrated High Surgical Risk Cohort, developed by pooling two registry data sets in a *post-hoc* manner, has major design and interpretation limitations.
5. The Duke Propensity Score Analysis was a retrospective, subset analysis with results that are difficult to interpret and where the matched cohorts do not represent any well defined population.

The panel believed that the following should be added to the indications for use:

- Change "too high risk" to "excessive risk;"
- Change indication to be for patients refractory to optimal medical therapy;
- Include anatomic appropriateness for repair using MitraClip in the indication;
- An experienced mitral valve surgeon/other members of a heart failure/heart team to determine the patient is not a surgical candidate; and
- Specify that the patient should have a 1 year life expectancy post procedure.

The majority of the panel found that there was not enough evidence to demonstrate a reasonable assurance of safety and effectiveness while some panel members believed that there is some evidence of safety and effectiveness in a sub-set of the patient population studied, although the panel could not define that specific sub-set.

The panel did not have specific feedback regarding the label, but did state that the indication for use, contraindications, warnings and precautions should be further developed based on the comments already provided by the panel.

The panel believed that freedom from mitral valve surgery should not be a primary effectiveness endpoint for a post-approval study stating that additional information should be collected. An appropriate endpoint might include death, heart failure hospitalization, and/or functional assessments such as 6 min walk test and cardiopulmonary stress testing (e.g. peak VO_2, RER).

Vote:

The panel voted on the safety, effectiveness, and risk benefit ratio of the MitraClip Delivery System.

On Question 1, the panel voted 8-0 that the data shows reasonable assurance that the Abbott Vascular MitraClip CDS is safe for use in patients who meet the criteria specified in the proposed indication.

On Question 2, the panel voted 4-5 that there is not reasonable assurance that the Abbott Vascular MitraClip CDS is effective for use in patients who meet the criteria specified in the proposed indication. (Chair voted as tie breaker)

On Question 3, the panel voted 5-3 that the benefits of the Abbott Vascular MitraClip CDS do outweigh the risks for use in patients who meet the criteria specified in the proposed indication.

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